EXHIBIT 24

[redacted]

Filed on behalf of: Junior Party **UNIVERSITY OF WESTERN AUSTRALIA**

Paper No. _____

Filed by: R. Danny Huntington – Lead Counsel
Sharon E. Crane, Ph.D. – Backup Counsel
Rothwell, Figg, Ernst & Manbeck, P.C.
607 14th St., N.W., Suite 800
Washington, DC 20005

Steven P. O'Connor, Ph.D. – Backup Counsel
Finnegan, Henderson, Farabow, Garrett & Dunner, LLP
Two Freedom Square, 11955 Freedom Drive
Reston, VA 20190-5675

William B. Raich, Ph.D. – Backup Counsel
Finnegan, Henderson, Farabow, Garrett & Dunner, LLP
901 New York Ave., N.W.
Washington, DC 20001

Date Filed: April 3, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT TRIAL AND APPEAL BOARD

University of Western Australia,
Junior Party
(Patent 8,455,636,
Inventors: Stephen Donald Wilton, Sue Fletcher and Graham McClorey)

v.

Academisch Ziekenhuis Leiden,
Senior Party
(Application 11/233,495
Inventors: Garrit-Jan Boudewijn van Ommen, Judith Christina Theodora van Deutekom, Johannes Theodorus den Dunnen and Annemieke Aartsma-Rus).

Patent Interference No. 106,007 (RES)
(Technology Center 1600)

UNIVERSITY OF WESTERN AUSTRALIA REPLY 1 (to AZL Opposition 1)

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Federal Cases

Federal Statutes

I. Precise Relief Requested

The University of Western Australia ("UWA") requests that the Board grant UWA Motion 1 that Academisch Ziekenhuis Leiden's ("AZL") Application No. 11/233,495 ("the '495 application") fails to provide adequate written description support for, and/or fails to enable, AZL's involved claims as required by 35 U.S.C. § 112(a).

II. Evidence in Support of the Reply

Appendix 1 is a list of exhibits cited in support of this Reply. The requirement for a statement of material facts has been waived. (*See* Paper 19 at 5.)

III. Argument

A. Dr. Sontheimer Is Not an Expert in the Technology at Issue

This interference is focused on exon skipping—the use of antisense oligonucleotides ("AONs") to induce the splicing machinery to "skip" exon 53 of the dystrophin pre-mRNA. These AONs are intended to treat patients with Duchenne Muscular Dystrophy ("DMD") by restoring production of dystrophin protein. Yet AZL has relied exclusively on (1) a technical expert with no experience in the pertinent field of exon skipping, Dr. Sontheimer, and (2) an inventor of AZL's '495 application, Dr. van Deutekom, who has a direct and substantial financial interest in AZL's applications. (*see* Ex. 2140 at 6, 7; Ex. 2141 at 14:4-15:23.)

Dr. Sontheimer has no experience in designing or using AONs to cause exon skipping. He has no scientific publications, no patents, and no patent applications directed to exon skipping. (Ex. 2122 at 15:17-23.) He has never given a scientific presentation on exon skipping. (*Id.* at 15:24-16:2.) He has never been involved in any exon skipping clinical trials. (*Id.* at 16:3-5.) Nor is he a medical doctor. (*Id*. at 15:12-14.) He is not an expert in DMD, nor has he done any work on dystrophin in his research. (*Id*. at 13:16-24.)

Atypically, Dr. van Deutekom spent nearly eight full pages of her declaration discussing Dr. Sontheimer's qualifications (Ex. 1125 at ¶¶ 4-18), even though she had never met or spoken to him prior to these proceedings and could not recall ever reading any of his publications or attending any scientific meeting where he was present. (Ex. 2141 at 38:6-39:12.) Dr. Sontheimer even admits that he does not satisfy the definition of a person of ***ordinary*** skill in the art proposed by UWA's expert Dr. Wood. (Ex. 2142 at 30:7-31:16; *see also* Ex. 2081 at ¶ 179.)

In contrast, UWA's expert, Dr. Wood, has extensive experience in conducting pre-clinical research in the discovery of therapeutic AONs for DMD as well as studying and treating patients with DMD using exon-skipping AONs. (Ex. 2003; Ex. 2081 at ¶¶ 7-10.) Given Dr. Sontheimer's lack of expertise in the relevant technology, where these two experts provide different opinions on the issues before the Board, UWA submits that the Board should credit the opinions of Dr. Wood over the opinions of Dr. Sontheimer.

B. Construction of AZL's Claims

It is undisputed that AZL's claims are exceedingly broad, potentially covering ***trillions*** of AONs with diverse lengths, sequences, chemical backbones, and internucleotide linkages. (Ex. 2081 at ¶¶ 382-93; Ex. 2142 at 99:13-22.) However, AZL disputes UWA's position that certain claim terms, discussed below, are indefinite.

1. "induces exon 53 skipping" and "capable of . . . inducing skipping of exon 53"

All of the claims of AZL's '495 application require that the claimed AONs either are "capable of . . . inducing skipping of exon 53" or "induce[] exon 53 skipping." (Ex. 2045.) But AZL's claims fail to recite a cell type, cell source, and conditions for assessing skipping, even though it is undisputed that ***all*** of these parameters significantly influence exon skipping. (Ex. 2081 at ¶¶ 66-67, 78, 403, 458-61; Ex. 2142 at 106:15-22.) Additionally, AZL's claims do not

require a level of exon skipping that must be achieved, even though inefficient or inconsistent AONs would not be useful. (Ex. 2045; Ex. 2081 at ¶ 458; Ex. 2142 at 127:22-128:24.)

In response, AZL contends that the claims should be construed to cover AONs that induce skipping "***regardless*** of the chosen method for detecting skipping or the level of detected skipping." (Ex. 1186 at ¶ 236.[1]) Further, AZL contends that "factors such as the level of therapeutic exon skipping, testing conditions, and transfection and cellular delivery methods are ***irrelevant*** to a person of ordinary skill's interpretation of the claims." (*Id.* at ¶ 236.) Still further, AZL contends that skipping is a "***binary limitation***," in that an AON either "induces exon 53 skipping to any degree that is detectable above background" (in which case the AON is covered), or it does not (in which case the AON is not covered). (*Id.* at ¶ 128.)

UWA respectfully submits that, in addition to creating written description and enablement issues, addressed below, AZL's proposed construction is contrary to the intrinsic record, as the AZL application at least discloses several different methods for both testing and evaluating skipping. (Ex. 1008 at 24:4-24, 27:17-28:5, 34:10-30.) Notably, although Table 2 of the '495 application identifies h53AON2 as "-" (negative) for inducing exon skipping, Dr. van Deutekom, a named inventor of the '495 application, insisted this was a function of the specific test conditions used, and that h53AON2 might induce skipping if tested at higher concentrations. (Ex. 2141 at 48:13-49:14.)

2. <u>"exon-internal sequence"</u>

Independent claims 78 and 100 of the '495 application recite that the claimed AON and/or h53AON1 are capable of binding to an "exon-internal sequence of exon 53." For purposes of this paper only, UWA will adopt AZL's construction of the term: "at a minimum,

[1] Unless otherwise indicated, all emphases are added.

the 'exon internal sequence' is the RNA sequence that is the complement of SEQ ID NO: 29, which Watson-Crick base pairing dictates is the sequence [3' GACAACGGAGGCCAAGAC 5']." (AZL Opp. 1 at 5.[2])

C. Lack of Written Description Support for AZL's Claims

1. AZL has failed to show possession of the claimed subject matter

When claims are directed to a genus, "a sufficient description . . . requires the disclosure of either [1] a representative number of species falling within the scope of the genus or [2] structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (en banc). Despite the enormous breadth of AZL's claims, it is undisputed that the AZL '495 application discloses just a ***single species*** of AON capable of inducing exon skipping within the scope of any of AZL's claims. (Ex. 2142 at 85:9-87:12.) Given the unpredictability of exon skipping and the substantial chemical variability of the compounds claimed (Ex. 2081 at §§ IV.F-H; *see also* § III.C.2, below), this does not adequately describe the claimed genus. *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1124-25 (Fed. Cir. 2008); *In re Curtis*, 354 F.3d 1347, 1358 (Fed. Cir. 2004).

AZL nevertheless contends that its claims are supported because the '495 application discloses h53AON1, which both "possesses a unique structure" and identifies "a corresponding complementary structure" of dystrophin exon 53. (AZL Opp. 1 at 7-8). AZL further contends that its broad genus claims are supported because "a person of ordinary skill would have

[2] The bracketed text provides the sequence that is the complement of SEQ ID NO: 29, which UWA believes AZL intended to recite, rather than the sequence of SEQ ID NO: 29 provided in AZL's paper. This error further illustrates the ambiguity with AZL's functional claim language.

routinely been able to extend the sequence of h53AON1 from 15-80 nucleotides" (even though h53AON1 is 18 nucleotides in length) "by making longer oligonucleotides complementary to the exon 53 mRNA sequence" (even though very few of AZL's claims are limited to complementary sequences). (*Id.* at 8.)

As an initial matter, h53AON1 is only 18 nucleotides in length, yet the claims cover AONs that range up to 50 or 80 unspecified nucleotides in length. h53AON1 is a 2'-O-methyl-phosphorothioate ("2-O-Me-PS") AON, yet the claims cover AONs with a great variety of chemical backbones and internucleotide linkages. h53AON1 contains only naturally-occurring RNA nucleobases, yet the claims cover AONs with DNA bases, other natural bases, and non-natural bases. And h53AON1 is perfectly complementary to the dystrophin pre-mRNA, yet the claims cover AONs containing mismatches. (Ex. 1008 at 3:17-20; Ex. 2081 at ¶¶ 278-326.)

The '495 application also ***fails to include*** any investigation of the purported target site bound by h53AON1. (Ex. 1008.) Indeed, as Dr. Sontheimer acknowledged, there is no instance in the AZL applications where the applicants "disclose the use of overlapping AONs to define targeted regions" and no instance "where they disclose the addition of one or more nucleotides after an active AON is identified." (Ex. 2122 at 37:21-38:7.) The focus of the '495 application, as illustrated in AZL's original claims, is the design of AONs that are partially complementary to both a predicted "open" and predicted "closed" secondary structure—the application has nothing to do with extending h53AON1 or any other AON to define a targeted region to induce exon skipping.[3] (Ex. 1007 at 53; Ex. 1008 at 1-2, 53; Ex. 2141 at 64:18-66:4.)

[3] Notably, the AZL application does not explain why h53AON2 failed to induce exon skipping. h53AON2 is the only other AON in the '495 application that was intended to target exon 53. (Ex. 2142 at 124:6-12.)

AZL also argues that the specification discloses modifications to the chemical backbone and internucleotide linkages that may be used, such as morpholinos, peptide nucleic acids (PNAs), and locked nucleic acids (LNAs). (AZL Opp. 1 at 7.) But although AZL's claims are exceedingly broad, all of the AONs disclosed in the '495 application, like h53AON1, use exclusively 2'-O-Me-PS modifications. (Ex. 1008 at 23, 26, 34; Ex. 2142 at 112:13-24, 132:4-11.) Moreover, Dr. Sontheimer couldn't recall ***any*** publications available as of March 2003 disclosing the use of AONs containing these modifications for exon skipping, and did not cite any such publications in his declarations. (Ex. 2142 at 113:14-114:16, 117:20-118:15.)

AZL's application also fails to disclose the use of non-natural nucleobases, DNA bases, and modified natural nucleobases. (*See* Ex. 1008.) While AZL contends that these modifications were "well-known in the art" and would have been understood to confer "useful and predictable properties" (AZL Opp. 1 at 11; Ex. 1186 at ¶ 153), the sole publication they rely on does not disclose anything about exon skipping and concludes that the particular nucleobase modification being studied conferred variable results for reasons that "are at present unclear." (Ex. 1211 at 3517; *see also* Ex. 2142 at 119:4-120:6, 121:13-24.)

The disclosure must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351.[4] In essence, AZL argues that this standard is met because the claims can be pieced together from disparate places in the specification, with deficiencies filled in based on the knowledge of the person of skill in the art. (*See* AZL Opp. 1 at 9-11; Ex. 2122 at 51:5-18.) But a "laundry list"

[4] Notably, none of Dr. Sontheimer's four declarations state what date he used for assessing written description for the '495 application, and he could not provide a date when asked about it at his deposition. (Exs. 1012, 1067, 1186, 2138; Ex. 2142 at 82:1-18.)

disclosure does not provide adequate written description support because it does not reasonably lead a skilled person to active compounds. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996). Moreover, "[i]t is ***not sufficient*** for purposes of the written description requirement of § 112 that the disclosure, when ***combined with the knowledge in the art***, would lead one to speculate as to modifications that the inventor might have envisioned, but failed to disclose." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Here, the claims are exceedingly broad, encompassing tremendous numbers of potential compounds, even though the specification discloses only a single species within the scope of any of AZL's claims. AZL cannot remedy these deficiencies by picking and choosing from a "laundry list" disclosure or by relying on the purported knowledge of persons of skill in the art.

2. Exon skipping was understood to be unpredictable

AZL makes several arguments, each flawed, alleging that exon skipping was understood as a predictable method as of the filing date of the AZL applications. AZL argues that the PTO's Written Description Guidance "recognize[s] a high level of skill in the [AON] art." (AZL Opp. 1 at 4.) But the cited example, Example 12, is not related to exon skipping, the technology at issue, and thus is immaterial as to whether or not the '495 application provides adequate written description support for its claims. (Ex. 1068.) Indeed, exon skipping seeks to increase levels of protein, while the antisense example in Example 12 seeks to reduce it—the precise opposite effect. (Ex. 1068 at 43-44.) UWA respectfully submits that the testimony of Dr. Wood, an expert with years of experience in the relevant field, coupled with the substantial body of contemporaneous scientific literature characterizing exon skipping as unpredictable, outweighs a single training example from a 2008 Guidance directed to substantially different technology.

AZL also relies on *Ex Parte Gleave and Miyake*, 2006 WL 6927761 (B.P.A.I. 2006) (Ex. 1207), an unpublished Board decision. (AZL Opp. 1 at 8.) But *Gleave* also did not involve

exon skipping. *See Gleave* at *2. Moreover, the *Gleave* application, unlike the '495 application, disclosed multiple working embodiments within the scope of the claims, a fact relied upon by the Board in its decision. *Id*. at *6-*7.

AZL also alleges that UWA's position regarding the unpredictability of exon skipping technology would "invalidate the rest of th[e] UWA patent family" as well as "the bulk—if not the entirety—of the patent portfolio of UWA's exclusive licensee, Sarepta Therapeutics Inc." (AZL Opp. 1 at 18.) Similarly, AZL argues that UWA's current position is "contrary to the ***implicit*** position it took in pursuing and obtaining genus claims in the other patents in this UWA patent family." (AZL Opp. 1 at 26-27.) But statements about predictability must be assessed independently for different patents with different filing dates and different disclosures. Indeed, "[p]redictability is a factual issue judged on a case-by-case basis." *Synthes USA, LLC v. Spinal Kinetics, Inc*. 734 F.3d 1332, 1344-45 (Fed. Cir. 2013) (explaining that the court's prior characterization of predictability of the field was not applicable); *see also Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254-56 (Fed. Cir. 2004) (finding that three priority applications each lacked adequate description by analyzing each application separately and considering the predictability of the art at the filing date of each application). AZL's focus on different patents having different disclosures and different filing dates is entirely immaterial to assessing the adequacy—or lack thereof—of AZL's disclosure.[5]

[5] Moreover, while AZL accuses UWA of having "implicit[ly]" contradicted itself, AZL has repeatedly taken inconsistent positions. For example, while AZL now argues that longer AONs would be predicted to be "more effective" and merely "fine-tuning" (Ex. 1012 at ¶ 54; Ex. 2141 at 96:21-99:3), AZL argued in 2013 that "there is evidence of unpredictability that oligonucleotides of different lengths act differently." (Ex. 2144 at 4; *see also* Ex. 2145 at 1

Citing *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005), AZL argues that UWA failed to consider "the predictability of the aspect at issue," because UWA presented evidence relating to exon skipping generally as opposed specifically to skipping of exon 53. (AZL Opp. 1 at 20-21.) As an initial matter, there is some incongruity in this accusation, as AZL seeks to wrap itself in PTO Training Materials and Board decisions that do not pertain to exon skipping at all, let alone skipping of exon 53. In any case, many of the statements relied upon by UWA are drawn from publications from the AZL group disclosing the same information that is disclosed in the '495 application. For example, the 2002 paper originally disclosing h53AON1 stated that "the effectivity of ***any designed AON, will therefore still have to be tested empirically in the cells*** . . . ." (Ex. 2010 at S76; Ex. 2081 at ¶ 70.) This contemporaneous recognition of the need to test each and every AON is also reflected in UWA's specification, which states that "[o]nce efficient exon skipping [has] been induced with one antisense molecule, subsequent overlapping antisense molecules ***may be synthesized and then evaluated***." (Ex. 1001 at 33:11-14.)

Other AZL papers document this unpredictability. A 2007 paper stated that "several years after the first attempts at dystrophin exon skipping with AOs [AONs], ***there are still no clear rules to guide investigators in their design***, and in mouse and human muscle cells ***in vitro there is great variability for different targets and exons***."[6] (Ex. 2013 at 807; Ex. 2081 at ¶ 71.) This paper directly compared AONs disclosed in the AZL applications versus those disclosed in the UWA patents, and concluded by stating that "the results of our study all indicated the

---

(arguing that "it is not always justified to increase the length of an oligonucleotide and assume that the longer oligonucleotide would be more efficient than the shorter one."))

[6] Despite co-authoring this paper, Dr. van Deutekom now contends that she disagrees with the quoted statement. (Ex. 2141 at 82:3-84:9.)

superiority" of the UWA AON now known as eteplirsen. (Ex. 2013 at 803, 808.) Similarly, a 2009 publication from AZL evaluated a series of AONs disclosed in the '495 application with AONs containing additional nucleotides and those prepared as PMOs. In some cases, the shorter AONs were more effective; in some cases, the longer AONs were more effective; in some cases only the PMOs were effective. (Ex. 2020 at 259.) UWA submits that AZL's papers, as well as the additional evidence set forth in ¶¶ 68-108 of Dr. Wood's first declaration, are both relevant and probative evidence as to the understanding of persons of skill in the art during the relevant period, and compares favorably with AZL's *ex post* analysis.

AZL also contends that Dr. Wood has taken positions in this interference about predictability inconsistent with those he published in 2010. (AZL Opp. 1 at 24.) But the purported inconsistencies fail under closer scrutiny. For example, Dr. Wood explained that his 2010 publication, titled "Toward an Oligonucleotide Therapy for [DMD]: A Complex Development Challenge," merely compared the relative difficulty in designing AONs in 2010 for single exon skipping versus designing those for exon inclusion or multi-exon skipping. (Ex. 1116; Ex. 2146 at 79:12-81:5.) In any case, developments illustrating the purported predictability of the art after the filing date—in this case in 2010—"are of ***no significance*** regarding what one skilled in the art believed as of [the filing] date." *In re Wright*, 999 F.2d 1557, 1562-63 (Fed. Cir. 1993). In contrast, public recognition of the unpredictability of the art after the filing date, such as the post-filing date statements of the AZL co-inventors, confirms that the field was viewed as unpredictable as of the filing date of the '495 application.

Finally, AZL argues that testing performed by Dr. van Deutekom "is contrary to UWA's assertion as to unpredictability, and confirms that AZL's specification . . . is enabling." (AZL Opp. 1 at 29.) As an initial matter, AZL's testing is irrelevant for written description purposes,

as it comes too late to demonstrate possession of the invention as of the filing date. *Ariad*, 598 F.3d at 1355 (evidence of what one of ordinary skill in the art knew after the filing date is "legally irrelevant to the question of whether the disclosure of the [application] conveys to those skilled in the art that the inventors were in possession of the claimed [invention]."). Moreover, AZL tested a limited number of ***non-representative species***, in that all five of the tested AONs were 2'-O-Me-PS containing exclusively naturally-occurring RNA nucleobases. (Ex. 2142 at 146:9-18, 147:5-11, 148:10-14.) This is significant, because incorporating chemical backbone, internucleotide linkage, and nucleobase modifications into an AON can all impart significantly different binding properties, as acknowledged by AZL's expert. (Ex. 2081 at ¶¶ 62-63, 80; Ex. 2142 at 122:22-123:7.) This further undermines the relevance of AZL's testing. *See AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299-1300 (Fed. Cir. 2014) (affirming finding of lack of written description for broad claims, despite more than 200 disclosed examples, because the disclosed examples were not representative of the breadth of the genus). Additional methodologic defects with AZL's tests are discussed in § III.D below.

D. The '495 Application Fails to Enable a Skilled Person to Make and Use the Invention Without Undue Experimentation

The disclosure of the AZL applications would not enable a person of skill in the art to make and use the claimed inventions without undue experimentation. It is undisputed that the various claims of the '495 application potentially cover a tremendous number of AONs with significant chemical variability, but the applications disclose just a single AON capable of inducing *in vitro* skipping for exon 53. The quantity of experimentation required to determine which AONs are capable of inducing exon 53 skipping *in vitro* is undue.

AZL nevertheless argues that the '495 application meets the "how to make" part of the enablement requirement because it discloses h53AON1, a 2'-O-Me-PS that was purportedly

designed by the inventors and synthesized by a third party vendor called Eurogentec. (AZL Opp. 1 at 12.) But AZL's claims are not limited to h53AON1 or even 2'-O-Me-PS AONs, but instead cover potentially trillions of different AONs with diverse nucleobase sequences, lengths, chemical backbones, and internucleotide linkages. As AZL's expert admits, "there would have been synthetic challenges" in making many of the AONs covered by the claims, there is no disclosure of how to synthesize AONs in the AZL applications, and there is no evidence that many such AONs were commercially available in 2003. (Ex. 2122 at 80:10-81:22.)

AZL also argues that the '495 application meets the "how to use" part of the enablement requirement because Example 1 teaches the use of h53AON1 to induce exon 53 skipping in cultured myoblasts, and Example 3 teaches the use of an AON that is 50 nucleotides in length (albeit, one outside the scope of the claims) to induce skipping (albeit, of multiple other exons). (AZL Opp. 1 at 12-13.) This sidesteps the issue entirely, because it fails to address the breadth of the claims. Even leaving synthesis challenges aside, it is undisputed that testing a single AON under the conditions set forth in the AZL '495 application takes weeks. (Ex. 2122 at 82:3-10; Ex. 1008 at 26-28.) Because exon skipping is unpredictable, practicing the full scope of the claimed invention would require exhaustive and undue synthesis and testing. (Ex. 2116 at ¶¶ 235-41.)

AZL's proposed "binary" claim construction—which classifies as positive any AON that induces any skipping above background in any cell type under any testing conditions—exacerbates the situation, because any AON producing a "negative result" would need to be evaluated under a multitude of testing conditions to confirm that it does not induce skipping. (Ex. 1186 at ¶¶ 128, 236.)

The limited testing performed for these interferences by Dr. van Deutekom illustrates the challenge. In November, Dr. van Deutekom instructed her team of ***eight people*** to conduct exon

skipping studies of a total of just ten AONs. (Ex. 2141 at 32:3-22; Ex. 2142 at 146:9-15.) Although these hand-selected AONs represent a tiny and non-representative fraction of what AZL claims, Dr. Van Deutekom nevertheless significantly altered the testing protocol from that disclosed in the application (for example, by using immortalized cells not disclosed in the AZL applications) (Ex. 2141 at 127:1-18); omitted standard controls such as use of scrambled AONs (Ex. 2141 at 109:17-22); and neglected to use sequence analysis, even though sequencing is routinely used in AZL's publications and in the AZL '495 application to confirm that exon skipping occurred (*compare* Ex. 2142 at 149:5-13 *with* Ex. 1008 at 39, Fig 1. *and* Ex. 2018 at 909, Fig. 1.) In *Wyeth and Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013), the court held that "expert testing performed in the course of litigation" was ***not sufficient*** to overcome an enablement challenge where the genus comprised potentially tens of thousands of candidate compounds and the specification disclosed only one. *Id*. at 1385. Here, AZL's claims potentially encompass trillions of compounds, the compounds at issue are large and diverse, the specification discloses only a single example, and testing each compound requires significant time and effort. (Ex. 2081 at ¶¶ 302, 407, 409-410, 422-427.)

Additionally, AZL makes several legal errors in evaluating enablement. First, AZL argues that UWA "has not presented evidence showing why the specification does not provide sufficient guidance for making h53AON1." (AZL Opp. 1 at 16.) But rather than claiming h53AON1, AZL chose to craft broad claims encompassing trillions of possible AONs. UWA's evidence goes to the inadequacy of the specification as it relates to the instant claims, not just h53AON1. A patent applicant "chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *MagSil Corp. v. Hitachi Global Storage Techs., Inc*., 687 F.3d 1377, 1381 (Fed. Cir. 2012). Second, AZL argues that UWA has

not "show[n] that experimentation to determine activity of h53AON1 (or any AON) in this case would be excessive (or undue), *e.g.*, that it would involve testing for an unreasonable length of time." (AZL Opp. 1 at 16-17.) But the problem is not how long it would take to make and test any particular single compound, but rather that each chemically distinct compound within the scope of the claims must be separately synthesized and empirically tested. "The resulting need to engage in a systematic screening process for each of the many . . . candidate compounds is excessive experimentation." *Wyeth*, 720 F.3d at 1386. Third, in evaluating undue experimentation, AZL's expert considered only whether "***any individual embodiment***" would require a test "that goes beyond what a person of skill in the art could do routinely." (Ex. 2142 at 83:13-84:5.) But "breadth of the claims" is an essential part of evaluating undue experimentation, particularly where, as here, AZL contorts its disclosure in an effort to cover promising DMD treatments invented and developed by others. *See Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997) (holding claims invalid for lack of enablement where the patentee had attempted "to dominate someone else's solution of the problem.")

E. The '495 Application Fails to Describe or Enable Therapeutically Useful AONs

AZL argues that therapeutic activity need not be established because its claims do not require a therapeutically useful result. (AZL Opp. 1 at 11-12.) Importantly, however, treatment of DMD is the sole disclosed practical utility for the AONs disclosed in the '495 application—yet no *in vitro* models of exon skipping are known to correlate with therapeutic activity and no known exon skipping therapies are commercially available. (Ex. 2041 at [0015-0017]; Ex. 2081 at ¶¶ 87-89; 428-433.) This situation fundamentally differs from those involving structural analogs of known active agents, or those involving *in vitro* assays known to correlate with

clinical activity. *Cf*. *In re Jolles*, 628 F.2d 1322, 1327-28 (C.C.P.A. 1980) (the claimed analogs had similar activity to a structurally-related known anticancer agent); *In re Brana*, 51 F.3d 1560, 1565 (Fed. Cir. 1995) (the claimed compounds showed activity in mouse cell lines used as proxies for leukemias). Because exon skipping is a nascent technology, the failure of the phase III clinical trial for drisapersen (h51AON1) is necessarily magnified in evaluating the description and usefulness under § 112(a) of the subject matter claimed by AZL.

AZL's proposed claim constructions again exacerbate this deficiency. By interpreting the claims to cover any AONs provided that they "induce exon 53 skipping to any degree that is detectable above background," *see* § III.B.1 above, AZL's claims encompass vast numbers of AONs that are not therapeutically useful, even if *in vitro* conditions can be manipulated such that some small amount of skipping is observed. Notably, AZL has repeatedly argued that AONs must be "sufficiently active" in appropriate "cellular model[s]" to be useful. (*E.g*., Ex. 2147 at 2-4; Ex. 2148 at 2-4; Ex. 2133 at 5-6; *see* Ex. 1012 at ¶ 138.)

The law is abundantly clear that, at a minimum, there needs to be a correlation between what is claimed and what is actually useful:

> If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. . . . That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis.

Rasmusson v. SmithKline Beecham Corp., 413 F.3d 1318, 1325 (Fed. Cir. 2005). AZL has done nothing more than initiate the search.

IV. Conclusion

For the reasons explained above and in UWA's Motion 1 (Paper No. 31), UWA respectfully requests that the Board hold that the '495 application fails to provide adequate written description support for, and/or fails to enable, AZL's involved claims.

Respectfully submitted,

Dated: April 3, 2015

By: */s/ R. Danny Huntington*

R. Danny Huntington, Reg. No. 27,903
Sharon E. Crane, Ph.D., Reg. No. 36,113
Rothwell, Figg, Ernst & Manbeck, P.C.
607 14th St., N.W., Suite 800
Washington, DC 20005

Steven P. O'Connor, Ph.D., Reg. No. 41,225
Finnegan, Henderson, Farabow, Garrett & Dunner, LLP
Two Freedom Square, 11955 Freedom Drive
Reston, VA 20190-5675

William B. Raich, Ph.D.
Finnegan, Henderson, Farabow, Garrett & Dunner, LLP
901 New York Ave., N.W.
Washington, DC 20001

Counsel for Junior Party
University of Western Australia

APPENDIX 1
List of Exhibits

EXHIBIT	***DESCRIPTION***
1001	UWA's U.S. Patent No. 7,807,816.
1007	AZL's WO 2004/083432 (the published AZL PCT Application, "Van Ommen" or "VO").
1008	AZL's U.S. Patent Application 11/233,495 (as-filed).
1012	Expert Declaration of Dr. Erik Sontheimer.
1068	USPTO Written Description Training Materials, Revised March 25, 2008, Example 12.
1116	Wood, "Toward an Oligonucleotide Therapy for Duchenne Muscular Dystrophy: A Complex Development Challenge," Science Translational Medicine, Vol. 2, No. 25, pp. 1-6 (March, 2010).
1125	Declaration of Judith van Deutekom.
1186	3rd Declaration of Erik J. Sontheimer, Ph.D.
1207	Decision on Appeal, Ex Parte Martin Gleave and Hideaki Miyake, Appeal No. 2005-2447, Appl. No. 09/619,908 (January 31, 2006) (2009 WL 6927761 (Bd. Pat. App. & Interf.).
1211	Flanagan et al., "A cytosine analog that confers enhanced potency to antisense of oligonucleotides," Proc. Nat'l Acad. Sci. USA, Vol. 96, pp. 3513-3518 (March, 1999).
2003	CV of Matthew J.A. Wood.
2004	S. J. Errington et al., "Target selection for antisense oligonucleotide induced exon skipping in the dystrophin gene," *J. Gene Med.*, **5(6)**:518-527 (2003).
2005	A. G. Douglas et al., "Splicing therapy for neuromuscular disease," *M. Cell. Neurosc.*, **56**:169-185 (2013).
2006	D. A. Braasch et al., "Novel antisense and peptide nucleic acid strategies for controlling gene expression," *Biochemistry*, **41(14)**:4503-4510 (2002).
2007	A. A. Koshkin et al., "LNA (Locked Nucleic Acids): Synthesis of the adenine, cytosine, guanine, 5-methylcytosine, thymine and uracil bicyclonucleoside monomers, oligomerisation, and unprecedented nucleic acid recognition," *Tetrahedron*, **54(14)**:3607-3630 (1998).
2008	J. Summerton et al., "Morpholino antisense oligomers: design, preparation, and properties." *Antisense Nucleic Acid Drug Dev.*, **7(3)**:187-195 (1997).
2009	D. A. Braasch et al., "Locked nucleic acid (LNA): fine-tuning the recognition of DNA and RNA." *Chem. Biol.*, **8(1)**:1-7 (2001).
2010	A. Aartsma-Rus et al., "Targeted exon skipping as a potential gene correction therapy for Duchenne muscular dystrophy." *Neuromuscul. Disord.*, **12**:S71-S77 (2002).
2011	S. M. Hammond et al., "Correlating In Vitro Splice Switching Activity With Systemic In Vivo Delivery Using Novel ZEN-modified Oligonucleotides," *Mol. Ther.-Nucleic Acids*, 2014 (in press).
2012	J. C. Van Deutekom et al., "Antisense-induced exon skipping restores dystrophin expression in DMD patient derived muscle cells," *Hum. Mol. Genet.*, **10(15)**:1547-1554 (2001).

EXHIBIT	***DESCRIPTION***
2013	V. Arechavala-Gomeza et al., "Comparative analysis of antisense oligonucleotide sequences for targeted skipping of exon 51 during dystrophin pre-mRNA splicing in human muscle," *Hum. Gene Ther.*, **18(9)**:798-810 (2007).
2014	A. Aartsma-Rus et al., "Guidelines for antisense oligonucleotide design and insight into splice-modulating mechanisms," *Mol. Ther.*, **17(3)**:548-553 (2009).
2015	B. Wu et al., "Targeted skipping of human dystrophin exons in transgenic mouse model systemically for antisense drug development," *PloS one*, **6(5)**:e19906 (2011).
2016	A. Aartsma-Rus et al., "Functional analysis of 114 exon-internal AONs for targeted DMD exon skipping: indication for steric hindrance of SR protein binding sites," *Oligonucleotides*, **15(4)**:284-297 (2005).
2017	C. J. Mann et al., "Improved antisense oligonucleotide induced exon skipping in the mdx mouse model of muscular dystrophy," *J. Gene Med.*, **4(6)**:644-654 (2002).
2018	A. Aartsma-Rus et al., "Therapeutic antisense-induced exon skipping in cultured muscle cells from six different DMD patients," *Hum. Mol. Genet.*, **12(8)**:907-914 (2003).
2019	C. T. Fragall et al., "Mismatched single stranded antisense oligonucleotides can induce efficient dystrophin splice switching," *BMC Med. Genet.*, **12(1)**:141 (2011).
2020	H. A. Heemskerk et al., "In vivo comparison of 2′-O-methyl phosphorothioate and morpholino antisense oligonucleotides for Duchenne muscular dystrophy exon skipping," *J. Gene Med.*, **11(3)**:257-266 (2009).
2021	Isis Pharmaceuticals Website: <http://www.isispharm.com/Pipeline/Therapeutic-Areas/Other.htm>
2022	C. A. Stein, “Delivery of antisense oligonucleotides to cells: a consideration of some of the barriers,” *Chemistry Today*, **32**:4-7 (2014).
2023	C. J. Mann et al., "Antisense-induced exon skipping and synthesis of dystrophin in the mdx mouse," *Proc. Natl. Acad. Sci.*, **98(1)**:42-47 (2001).
2024	M. Bremmer-Bout et al., "Targeted exon skipping in transgenic hDMD mice: A model for direct preclinical screening of human-specific antisense oligonucleotides," *Mol. Ther.*, **10(2)**:232-240 (2004).
2025	F. Muntoni et al., "128th ENMC International Workshop on ‘Preclinical optimization and Phase I/II Clinical Trials Using Antisense Oligonucleotides in Duchenne Muscular Dystrophy’ 22–24 October 2004, Naarden, The Netherlands," *Neuromuscul. Disord.*, **15(6)**:450-457 (2005).
2026	C. A. Stein et al., "Therapeutic oligonucleotides: the road not taken," *Clin. Cancer Res.*, **17(20)**:6369-6372 (2011).
2027	T. L. Jason et al., "Toxicology of antisense therapeutics," *Toxicol. Appl. Pharmacol.*, **201(1)**:66-83 (2004).
2028	K. Anthony et al., “Dystrophin quantification, Biological and translations research implications,” *Neurology*, **83**:1-8 (2014) (on-line preprint).
2029	X. Tian et al., "Imaging oncogene expression," *Ann. N. Y. Acad. Sci.*, **1002(1)**:165-188 (2003).

EXHIBIT	***DESCRIPTION***
2030	P. A. 't Hoen et al., "Generation and characterization of transgenic mice with the full-length human DMD gene," *J. Biol. Chem.*, **283(9)**:5899-5907 (2008).
2031	L. J. Popplewell et al., "Comparative analysis of antisense oligonucleotide sequences targeting exon 53 of the human DMD gene: Implications for future clinical trials," *Neuromuscul. Disord.*, **20(2)**:102-110 (2010).
2032	E. Kaye, "Results of the Eteplirsen Phase 2b and Phase 2b Extension Study in Duchenne Muscular Dystrophy," Abstract for 8th Annual Meeting of the Oligonucleotide Therapeutics Society (2012).
2033	S. Cirak et al., "Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study," *Lancet*, **378(9791)**:595-605 (2011).
2034	Sarepta Therapeutics Press Release dated January 15, 2014.
2035	U.S. Patent Application Publication No. 2014/0213635.
2036	N. M. Goemans et al., "Systemic administration of PRO051 in Duchenne's muscular dystrophy," *N. Engl. J. Med.*, **364(16)**:1513-1522 (2011).
2037	T. Voit et al., "Safety and efficacy of drisapersen for the treatment of Duchenne muscular dystrophy (DEMAND II): an exploratory, randomised, placebo-controlled phase 2 study," *Lancet Neurol.*, **13(10)**:987-96 (2014).
2038	K. M. Flanigan et al., "Pharmacokinetics and safety of single doses of drisapersen in non-ambulant subjects with Duchenne muscular dystrophy: Results of a double-blind randomized clinical trial," *Neuromuscul. Disord.*, **24(1)**:16-24 (2014).
2039	Prosensa Press Release dated September 20, 2013.
2040	GlaxoSmithKline Press Release dated January 13, 2014.
2041	U.S. Patent Application Publication No. 2006/0147952.
2042	International Patent Application No. PCT/NL2003/000214.
2043	U.S. Patent Application Publication No. 2013/0072671.
2044	Updated Filing Receipt mailed December 11, 2012, In U.S. Patent Application No. 13/550,210.
2045	Academish Ziekenhuis Leiden Clean Copy of Claims and Sequences submitted August 5, 2014, in Interference No. 106,007 (RES).
2046	U.S. Patent No. 8,455,636.
2047	Academish Ziekenhuis Leiden Clean Copy of Claims and Sequences submitted August 5, 2014, in Interference No. 106,008 (RES).
2048	U.S. Patent No. 7,807,816.
2049	U.S. Patent No. 7,960,541.
2050	Academish Ziekenhuis Leiden Clean Copy of Claims and Sequences submitted October 15, 2014, in Interference No. 106,013 (RES).
2051	U.S. Patent No. 8,486,907.
2052	U.S. Patent Application Publication No. 2014/0275212.
2053	Amendment Under 37 C.F.R. §1.312 - Notice of Allowance Mailed, dated September 19, 2014, submitted in U.S. Patent Application No. 14/248,279.

EXHIBIT	***DESCRIPTION***
2054	Excerpts from the prosecution history of U.S. Patent Application No. 11/233,495.
2055	Excerpts from the prosecution history of U.S. Patent Application No. 13/550,210.
2056	Excerpts from the prosecution history of U.S. Patent Application No. 14/198,992.
2057	Excerpts from the prosecution history of U.S. Patent Application No. 14/248,279.
2058	J. R. Mendell et al., "Eteplirsen for the Treatment of Duchenne Muscular Dystrophy," *Ann. Neurol.*, **74**:637-647 (2013).
2059	J. R. Mendell et al., "Eteplirsen in Duchenne Muscular Dystrophy (DMD: 144 Week Update on Six-Minute Walk Test (6MWT) and Safety," presented at the 19th International Congress of the World Muscle Society, October 7-11, 2014, Berlin, Germany.
2060	GlaxoSmithKline Press Release dated January 19, 2011.
2061	P. Järver et al., "A Chemical View of Oligonucleotides for Exon Skipping and Related Drug Applications," *Nucleic Acid Therapeutics*, **24(1)**:37-47 (2014).
2062	Second Preliminary Amendment filed on January 3, 2013, in U.S. Patent Application No. 13/550,210.
2063	Response & Amendments filed on January 21, 2014, in U.S. Patent Application No. 13/550,210.
2064	Response & Amendments filed on May 12, 2014, in U.S. Patent Application No. 13/550,210.
2065	Claims from Application filed on December 22, 2010, in U.S. Patent Application No. 12/976,381.
2066	Preliminary Amendment filed on December 22, 2010, in U.S. Patent Application No. 12/976,381.
2067	Preliminary Amendment filed on November 7, 2008, in U.S. Patent Application No. 12/198,007.
2068	Claims from Application filed on September 21, 2005, in U.S. Patent Application No. 11/233,495.
2069	Preliminary Amendment filed on September 21, 2005, in U.S. Patent Application No. 11/233,495.
2070	Amendment filed on October 31, 2007, in U.S. Patent Application No. 11/233,495.
2071	Amendment filed on April 1, 2009, in U.S. Patent Application No. 11/233,495.
2072	Amendment filed on September 16, 2009, in U.S. Patent Application No. 11/233,495.
2073	Amendment After Non-Final Action filed on June 24, 2010, in U.S. Patent Application No. 11/233,495.
2074	Amendment In Response to Advisory Action filed on March 14, 2011, in U.S. Patent Application No. 11/233,495.
2075	Excerpts from Antisense Drug Technology: Principles, Strategies, and Applications (Stanley T. Crooke ed., Marcel Dekker, Inc.) (2001).

EXHIBIT	***DESCRIPTION***
2076	Applicant -Initiated Interview Summary and Notice of Allowance filed on May 19, 2014, in U.S. Patent Application No. 13/550,210.
2077	Amendments to the Claims filed on May 8, 2014, in U.S. Patent Application No. 11/233,495.
2078	Amendments to the Claims filed on May 12, 2014, in U.S. Patent Application No. 13/550,210.
2079	Amendments to the Claims filed on July 16, 2014, in U.S. Application No. 14/198,992.
2080	Office Action filed on September 27, 2013, in U.S. Patent Application No. 13/550,210.
2081	Declaration of Matthew J. A. Wood, M.D., D. PHIL.
2082	Sarepta Therapeutics Press Release dated August 15, 2011.
2083	Kinali et al., "Local restoration of dystrophin expression with the morpholino oligomer AVI-4658 in Duchenne muscular dystrophy: a single-blind, placebo-controlled, dose-escalation, proof-of-concept study," *Lancet Neurology*, **8**:918-928 (Oct. 2009).
2084	Response filed on October 21, 2014, in EP12198517.
2085	Response filed on June 26, 2014, in EP13160338.
2086	U.S. Patent Application No. 14/198,992of AZL as filed.
2087	U.S. Patent Application No. 13/550,210 of AZL and Preliminary Amendment as filed.
2088	U.S. Patent Application Publication No. 2013/0072671 of AZL.
2089	U.S. Patent Application No. 12/976,381 of AZL and Preliminary Amendment as filed.
2090	U.S. Patent Application Publication No. 2011/0312086 of AZL.
2091	U.S. Patent No. 8,759,507 of AZL.
2092	U.S. Patent Application No. 12/198,007of AZL as filed.
2093	U.S. Patent Application Publication No. 2009/0076246 of AZL.
2094	U.S. Patent No. 7,534,879 issued on May 19, 2009 to AZL.
2095	U.S. Patent Application No. 11/233,495 of AZL and Preliminary Amendment as filed.
2096	Terminal Disclaimer filed on July 15, 2014, in the AZL U.S. Application No. 14/198,992 over the AZL U.S. Application No. 13/550,210.
2097	Preliminary Remarks filed on March 6, 2014, in the AZL U.S. Patent Application No. 14/198,992.
2098	U.S. Patent Application No. 13/270,992 of UWA, Transmittal and Preliminary Amendment as filed.
2099	U.S. Patent Application Publication No. 2012/0029060 of UWA.
2100	U.S. Patent Application No. 12/837,359 of UWA, Application Data Sheet and Preliminary Amendment as filed.
2101	U.S. Patent Application Publication No. 2011/0015253 of UWA.
2102	U.S. Patent No. 8,232,384 issued on July 31, 2012 to UWA.
2103	U.S. Patent Application No. 11/570,691 of UWA, Transmittal and Preliminary Amendment as filed.

EXHIBIT	***DESCRIPTION***
2104	U.S. Patent Application Publication No. 2008/0200409 of UWA.
2105	WO 2006/000057 of UWA.
2106	U.S. Patent No. 5,138,045.
2107	U.S. Patent No. 6,312,900.
2108	U.S. Patent Application No. 14/248,279 of AZL, Track One Request and Application Data Sheet as filed.
2109	Terminal Disclaimer filed on August 7, 2014, in the AZL U.S. Patent Application No. 14/248,279 over the AZL U.S. Patent Application No. 11/233,495.
2110	Remarks filed on August 27, 2014, in the AZL U.S. Patent Application No. 14/248,279.
2111	U.S. Patent Application No. 13/271,080 of UWA, Transmittal and Preliminary Amendment as filed.
2112	U.S. Patent Application Publication No. 2012/0022145.
2113	*Brown v. Fodor*, Interference No. 104,358, Paper No. 60 at p. 2 (BPAI 1999).
2114	Transcript of December 12, 2014 Teleconference with Administrative Patent Judge Schafer (rough draft).
2115	*EXHIBIT NUMBER NOT USED*
2116	Second Declaration of Matthew J. A. Wood, M.D., D. PHIL.
2117	Amendment dated January 22, 2014 in U.S. Application Serial No. 11/233,495.
2118	USPTO "2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting or Involving…Natural Products" ("the March Guidance").
2119	Interim Guidance on Patent Subject Matter Eligibility ("the December Guidance").
2120	Flanigan et al., "Rapid Direct Sequence Analysis of the Dystrophin Gene," *Am. J. Hum. Genet.* **72**:931-939 (2003).
2121	Wilton et al., "Antisense Oligonucleotide-induced Exon Skipping Across the Human Dystrophin Gene Transcript," *Molecular Therapy* **15(7)**:1288-1296 (2007).
2122	Transcript of the January 21, 2015 deposition of Erik J. Sontheimer, Ph.D.
2123	Doyle et al., "Inhibition of Gene Expression Inside Cells by Peptide Nucleic Acids: Effect of mRNA Target Sequence, Mismatched Bases, and PNA Length," *Biochemistry* **40**:53-64 (2001).
2124	List of Publications for Matthew J. A. Wood, M.D., D. PHIL.
2125	International Patent Application No. PCT/AU2000/00693 ("Wraight"), published as WO 00/78341 on December 28, 2000.
2126	UWA Clean Copy of Claims and Sequence, as filed in Interference No. 106,007 on August 1, 2014 (Paper 12).
2127	UWA Clean Copy of Claims and Sequence, as filed in Interference No. 106,007 on August 7, 2014 (Paper 12).
2128	Errata sheet for the January 22, 2015 deposition of Matthew J. A. Wood, M.D., D. PHIL.

EXHIBIT	***DESCRIPTION***
2129	Excerpts of SEC Form 8-K, dated November 23 2014, for BioMarin Pharmaceutical Inc.
2130	WO 2013/112053 A1.
2131	Mathews et al., "Expanded Sequence Dependence of Thermodynamic Parameters Improves Prediction of RNA Secondary Structure," **J. Mol. Biol. 288**:911-940 (1999).
2132	Mfold illustrations for Exon 51 and Exon 53 with varying amounts of intron sequence.
2133	Declaration of Judith C.T. van Deutekom Under 37 C.F.R. §1.132, filed on January 27, 2012, in U.S. Patent Reexamination Control No 90/011,320, regarding U.S. Patent No. 7,534,879.
2134	WO 2002/24906 A1 of AZL.
2135	Aartsma-Rus et al., "Antisense-induced exon skipping for duplications in Duchenne muscular dystrophy," *BMC Medical Genetics* **8**:43 (2007).
2136	Program Schedule for The Tenth Annual Meeting of the RNA Society, held at the Banff Centre for Conferences, in Banff, Alberta, Canada, from May 24-29, 2005.
2137	Poster Abstract Listing for The Tenth Annual Meeting of the RNA Society, held at the Banff Centre for Conferences, in Banff, Alberta, Canada, from May 24-29, 2005.
2138	Fourth Declaration of Erik Sontheimer, Ph.D. (Pursuant to Bd.R. 41.155(b)(2) and SO ¶¶ 155.1.3 and 155.1.4), dated March 9, 2015.
2139	Annotated scenario introduced and referred to during March 12, 2015 deposition of Erik J. Sontheimer, Ph.D.
2140	Valorization Memorandum published by the Dutch Federation of University Medical Centers in March 2009.
2141	Transcript of the March 11, 2015 deposition of Judith van Deutekom, Ph.D.
2142	Transcript of the March 12, 2015 deposition of Erik J. Sontheimer, Ph.D.
2143	Manual of Patent Examining Procedure 2308.02 (6th ed., rev. 3, July 1997).
2144	Applicant-Initiated Interview Summary dated April 8, 2013 in U.S. Application Serial No. 13/094,548.
2145	Reply to EPO Communication dated June 26, 2014 in European Application Serial No. 13160338.
2146	Transcript of the March 5, 2015 deposition of Matthew J. A. Wood, M.D., D. PHIL.
2147	Reply to EPO Communication dated October 23, 2014 in European Application Serial No. 12198485.
2148	Reply to EPO Communication dated October 21, 2014 in European Application Serial No. 12198517.
2149	Errata sheet for the March 12, 2015 deposition of Erik J. Sontheimer, Ph.D.

1

CERTIFICATE OF SERVICE

Pursuant to S.O. ¶ 105.3, I hereby certify that prior to 5:00 pm Eastern Time, on this 3rd day of April, 2015, the foregoing UNIVERSITY OF WESTERN AUSTRALIA REPLY 1 was served on counsel of record for Senior Party Academisch Ziekenhuis Leiden by being filed through the Interference Web Portal. In addition, prior to 6:00 pm Eastern Time, on this 3rd day of April, 2015, counsel of record for Senior Party Academisch Ziekenhuis Leiden was served via electronic mail.

/s/ Erik van Leeuwen
Erik van Leeuwen
Litigation Operations Coordinator
Rothwell, Figg, Ernst & Manbeck, P.C.